REMARKS

Claims 1, 10, 11, 15, 25, 29-32 and 35-69 are pending in this application. By this Amendment, claims 1, 40, 43, 46, 47, 55, 56, 60, 63 and 64 are amended, and claims 68 and 69 are added. No new matter is added by this Amendment. Support for the language added to claims 1, 46, 63 and 64 and support for new claims 68 and 69 can be found throughout the specification and original claims, as further discussed below.

Applicants appreciate the courtesies shown to Applicants' representatives by Examiner Baskar and Examiner Ungar in the June 25, 2007 personal interview. Applicants' separate record of the substance of the interview is incorporated into the following remarks.

New claims 68 and 69 are not taught or suggested by any of the applied references, which teach use of monocytes that have at best a dilution effect on *Tropheryma whippelii* due to the fact that its doubling time is greater than that of monocytes. The claim amendments and new claims 68 and 69 further respond to the Examiners' suggestions in the June 25, 2007 personal interview.

I. Interview Summary

During the June 25, 2007 interview, Examiner Ungar requested that applicants point out support in the specification for some of the claim language. As agreed at the interview, claim limitations are adequately supported if they appear literally in, or "naturally flow" from, the disclosure found in the original application.

A. "Reproducibly and Detectably" Multiplying for "At Least 72 Days" as Recited in Claim 1

The specification provides sufficient support for the recitation of the bacterium reproducibly and detectably multiplying over time in the culture medium for at least 72 days.

The recitation "the bacterium can reproducibly and detectably multiply over time in the culture medium for at least 72 days" naturally flows from the original specification. For

example, the specification at page 2, lines 14-17 describes that "the inventors have discovered that the cell culture which enables the *Tropheryma whippelii* bacterium to be isolated and multiplied must have both a long lifetime and a slow multiplication time. They have in fact demonstrated that the doubling time of the bacterium is very long (18 days)." Further, representative Example 1 discloses that no cytopathogenic effect was detected before day 65, and on day 72 small, dark and irregular inclusion could be detected by inverted microscopy. See page 16, lines 16-19 of the specification. According to representative Example 2, on day 75, the bacteria detected on day 72 were used to inoculate a confluent cellular mat in a culture dish. Every ten days, for thirty days, the bacteria were subcultured. The propagation method proved to be efficient because the bacteria were found after thirty days of subculture. See Table 1, and Example 2 of the specification.

In addition, in describing the invention without limitation to any strain, page 2, lines 28-31 of the specification refer to fibroblasts (to be used for culturing the *Tropheryma whippelii* bacterium) being kept alive "for several months." This implies that the culture would live for several months along with those cells, or the information would be irrelevant. Also, original claim 1 refers to the *Tropheryma whippelii* bacterium "isolated and established in culture." The term "established in culture" is defined at page 3, lines 3-5 of the specification as "meaning that the bacterium is obtained reproducibly and multiplies over time, especially via successive subcultures on a cell culture." In its original language, the expression "multiply over time" refers to the bacterium being maintained in culture indefinitely.

The disclosure of the present application can be attributed to the invention of a culture comprising the medium and the *Tropheryma whippelii* bacterium as recited in claim 1 and disclosed in the specification, and not just the species of the Examples. A patentee is entitled

to broad claims which define the invention without reference to a particular embodiment. See, for example, In re Anderson, 471 F.2d 1237 (CCPA 1973).

The specification, in its entirety, including the representative examples, clearly describes that the long doubling time of the *Tropheryma whippelii* bacterium requires a culture medium that will sustain the multiplication of the bacterium, and it does so for at least 72 days as expressly mentioned in Examples 1 and 2.

Moreover, the recitation that the bacterium is detectable for at least 72 days is definite. Example 1 describes that the bacteria were detected on day 72 by inverted microscopy. Example 3 discloses that the bacteria were detected by immunofluorescence on day 105. As requested by Examiner Ungar, claim 1 has been amended to recite a disclosed method of "detection." Specifically, claim 1 has been amended to recite that the bacterium can reproducibly and detectably multiply over time in the culture medium for at least 72 days as detected by inverted microscopy.

The specification thus provides support for the recitation of the bacterium reproducibly and detectably multiplying over time in the culture medium for at least 72 days as detected by inverted spectroscopy, as recited in claim 1.

B. Culture Medium

As discussed during the interview, claim 1 encompasses a medium that may or may not include cells.

As discussed at length during the interview, one of ordinary skill in the art understands that a bacterium can be cultured in a medium having cells or a medium not having cells. Moreover, the present specification variously refers to a "culture" and a "cell culture." This would imply that the culture may be other than a cell culture, for example, a culture comprising a medium without cells.

Thus, the original specification provides support for a culture medium including cells and a culture medium not including cells.

C. Claim 36

When discussing the important features of the present application, namely, that the culture medium must be capable of sustaining the growth of a bacterium that has a longer doubling time than most bacteria, Examiner Ungar agreed that the dividing time of the cells in the culture medium in combination with *Tropheryma whippelii* bacterium appears to distinguish the claimed culture from the prior art.

During the interview, Examiner Ungar requested that the support in the original specification for claim 36 be pointed out.

The disclosure at page 2, lines 14-27 indicates that the dividing time of any cells in which the *Tropheryma whippelii* bacterium is cultured must be greater than the doubling time of the bacterium. In particular, the specification explains that "the cell culture ... must have both a long lifetime and a slow multiplication time," and that "if the cells multiply too rapidly relative to the growth time of the bacterium, they cannot be cultivated because a dilution effect takes place and it becomes impossible to segregate the infected cells from non-infected cells." Thus, it is implicit that the cells must have a doubling time greater than that of the *Tropheryma whippelii* bacterium in order to satisfy these requirements and avoid a dilution effect.

New independent claim 68 recites the that the cell has a dividing time greater than the doubling time of the bacterium, rather the 72-day feature recited in claim 1. Similarly, new independent claims 69 recites that the cell is selected such that it does not multiply so rapidly relative to the growth of the bacterium as to cause a dilution effect of the bacterium, rather the 72-day feature recited in claim 1, in the literal terminology of the specification.

Moreover, those of ordinary skill in the art have recognized that *Tropheryma whippelii* bacterium have an unusually long doubling time. For example, "it has been recognized that the estimated bacterial doubling time [of the *Tropheryma whippelii* bacterium] was 18 days, which is longer than that of any other characterized bacterium." See Maiwald, et al., "Cultivation of *Tropheryma whippelii* from Cerebrospinal Fluid," Journal of Infectious Disease, vol. 188, at page 802 (September 15, 2003) (previously submitted to the Patent Office with the February 4, 2007 Amendment).

Maiwald further suggests that its authors observed a doubling time of 4 days for *Tropheryma whippelii*, still characterizing that time as "among the longest observed doubling time for any bacteria." Maiwald characterizes the difference in calculated doubling times as being "due either to the different measurement methods or culture conditions or to the difference between *Tropheryma whippeli* strains." In view of the potential variation in *Tropheryma whippelii* doubling times, which also decrease as a culture matures, but the continued fact that they are longer than those of the monocytes of the prior art, Applicants have eliminated references to doubling times from their independent claims.

Thus, in view of the disclosure as a whole and the unusually long doubling time of the *Tropheryma whippelii* bacterium, the recitations of claims 36, 68 and 69 are literally supported in and/or naturally flow from the original disclosure.

D. Claims 40 and 43

During the interview, Examiner Ungar suggested that claims 40 and 43 are redundant of the recitation of claim 1. Specifically, Examiner Ungar recognized that a bacterium of the same species as the deposited *Tropheryma whippelii* bacterium would necessarily be a bacterium responsible for Whipple's disease as recited in claim 1. Applicants have amended claims 40 and 43 to recite that the bacterium of those claims is specifically the deposited bacterium strain.

E. Conclusion

For at least the foregoing reasons, pending claims 1, 10, 11, 15, 25, 29-32 and 35-69 comply with the all of the requirements of 35 U.S.C. §112, first and second paragraphs, and are distinguished over the applied references. Namely, none of Schoedon, Muller, Drancourt, Kent, and Harlow and Lane, in combination or alone, teach or suggest all of the features recited in claims 1, 10, 11, 15, 25, 29-32 and 35-69.

II. Conclusion

In view of the foregoing, the Amendment filed on February 5, 2007, the Supplemental Amendment filed on May 17, 2007 and the personal interview conducted with Examiners Baskar and Ungar, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 1, 10, 11, 15, 25, 29-32 and 35-69 are earnestly solicited.

Should Examiners Baskar and Ungar believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

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